Amendments to the Drawings:

The drawing sheet attached in connection with the above-identified application containing Figure 1 is being presented as a new formal drawing sheet or sheets to be substituted for the previously submitted drawing sheet or sheets. The drawing Figure 1 has been amended. Appended to this amendment is an annotated copy of the previous drawing sheet which has been marked to show changes presented in the replacement sheet of the drawing.

The specific changes which have been made to Figure 1 are the inclusion of labels (A), (B) and (C) to better identify and distinguish the data presented therein.

REMARKS

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

Claims 1 and 10 are currently being amended. Support for this amendment can be found, *inter alia*, in paragraphs 1 and 22 of the specification. Claims 4 and 17 are being canceled without prejudice or disclaimer thereto.

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

After amending the claims as set forth above, claims 1-3 , 5-16 and 18 are now pending in this application, of which claims 5-9 are withdrawn from examination.

Objection to the Drawings

The Examiner objects to Figure 1 for allegedly failing to distinguish the identity of the frequency histograms presented in Figure 1. Amended Figure 1 is presented herewith to more clearly label the source of each histogram. Withdrawal of this objection in light of this amendment is respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph

The Examiner rejects claim 1-4 and 10-17 for allegedly failing to comply with the written description requirement. Specifically, the Examiner alleged that the claim encompass a genus of molecules based on a "wish to know" the identity of molecules with the biological properties recited in the claims. Applicants respectfully traverse this rejection as it may apply to the amended claims.

According to the USPTO's guidelines for determining adequacy of written description, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species. M.P.E.P. § 2163. The guidelines further note that "[w]hat constitutes a 'representative number' is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a 'representative number' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed." *Id.* Applicants submit that such a representative number species of the claimed genuses are disclosed in the instant specification.

First, the Examiner alleges that the instant specification only supported targeting peptides that comprised a tri-peptide motif *or* those peptides disclosed in U.S. Pat. Nos. 6,491,894, 6,528,481, 6,296,832 or 6,180,084, as well as sodium 1-(12-hydroxy)octadecanyl sulfate. Applicants respectfully submit that the referenced patents disclose numerous peptides, as evidence, for example, in Tables 1-3 of the '894 patent. Some of these peptides have tri-peptide motifs, such as NGR or RGD, and many others do not. Yet specific tumor targeting is nevertheless exhibited, as Examples II-VIII of the '894 patent demonstrates.

Additionally, the '481 patent discloses numerous angiogenic vasculature homing peptides, such as those provided in SEQ ID NOs: 1-16 of that patent. Likewise, the '832 patent lists tissue-specific peptides, such as those listed in Tables 1 and 2 of that patent. As dozens of peptides useful for targeting are presented, Applicants assert that the genus of a "peptide capable of targeting cells that are cancerous, tumor vasculature or neovasculature" is well supported by the disclosure. Further, a person of skill in the art would readily recognize additional targeting peptides that would be useful in the present invention, either presently known or developed through known, routine screening techniques, such as those disclosed in the '894 patent.

Similarly, the Examiner alleges that only one species of the immune response triggering portion is disclosed and the claimed genus is therefore not supported. Applicants disagree. In the interest of expediting prosecution and without acquiescing to the Examineri's rejection, the claims have been amended to recite "galactose-α-1,3-galactose which triggers a

complement mediated hyperacute immune response," and the specification recites both the method by which the carbohydrate is synthesized and a specific example of such a carbohydrate.

Because the claimed invention is fully described and supported by the specification, Applicants respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 102(b)

The Examiner rejects claims 1-3 under 35 U.S.C. § 102(b) for allegedly being anticipated by Corti (WO 01/61017) as evidenced by Yang (J. Exp. Med. 188:247-254 (1998)). Applicants traverse this rejection as it may apply to the amended claims.

An anticipation rejection under 35 U.S.C. § 102 requires a showing that each limitation of a claim is found in a single reference, practice or device. *See In re Donohue*, 766 F.2d 531 (Fed. Cir. 1985). In order for a reference to be anticipatory, it must "be enabling and describe the applicant's claimed invention sufficiently to have placed it in possession of a person of ordinary skill in the field of the invention." *See In re Paulson*, 30 F.3d (Fed. Cir. 1994). Applicants assert that the cited references do not anticipate the present claims as they do not teach each and every element of the claims.

As the Examiner discusses, Corti teaches TNF fusion proteins. It does not teach the use of an immune response triggering portion, which is galactose-α-1,3-galactose which triggers a complement mediated hyperacute immune response. Indeed, while TNF is a major player in one type of hyperacute immune response, it functions in a different pathway than complement and is not interchangeable. The reference cited by the Examiner, Yang, states that "TNF is one of the major players in hyperacute responses," but does *not* state that it has any role in the complement mediated hyperacute immune response. Yang, p. 252, col. 2. There are several mechanisms at work in the hyperacute immune reaction. One is the pro-inflammatory cytokines, such as TNF. Another is the complement-mediated responses, which generate the complement activation product, C5. Attached as an exhibit is an abstract

of Lentsch, *et al.*, Am. J. Pathol. 152:1327-1336 (1998), which clearly shows that during acute immune responses, TNF uses a NF-kB dependent pathway to mediate responses, while C5 does not utilize this pathway.

Additionally, Corti teaches conjugating an antibody or an antibody fragment to TNF. Page 6, lines 13-21. In the present application, however, Applicants disclose that antibody moieties actually inhibit a complement response in the present invention in paragraph 22. This further supports the distinction between the pathway activated in Corti and the complement mediate response of the present invention.

Because Corti does not teach each and every element of the claims, it cannot anticipate the claimed invention. Accordingly, Applicants respectfully request withdrawal of the rejection.

Rejections under 35 U.S.C. § 103(a)

To establish a *prima facie* case of obviousness, the Examiner must satisfy three criteria with respect to the cited combination of publications. First, there must be some motivation, evidenced in the prior art without resort to the present disclosure to modify or combine the references in the manner cited. Second, there must be a reasonable expectation of success in the cited combination or modification of the cited references. Finally, the cited reference(s) must teach each and every element of the claims. *In re Vaeck*, 947 F.2d 488 (Fed. Cir. 1991). Applicants respectfully assert that this burden has not been met.

Corti and Patierno

Claims 10-12 and 14-16 are rejected under 35 U.S.C. § 103(a) over Corti in view of Patierno (U.S. Pat. No. 6,288,039). Specifically, the Examiner alleges that the TNF-fusion proteins of Corti combined with the breast cancer diagnostic and treatment kit of Patierno render the presently claimed invention obvious. Applicants traverse this rejection as it may apply to the amended claims.

The deficiencies of Corti is discussed *supra*, particularly its failure to disclose galactose-α-1,3-galactose or indeed any complement-triggering portion. Patierno does not remedy this deficiency. Patierno discloses kits comprising immunohistochemical imaging reagents for diagnosing breast cancer, or for delivery of inhibitors of specific receptors. There is no disclosure of galactose-α-1,3-galactose or any complement-triggering portion. As the combination of these two references does not teach the presently claimed invention, they cannot render the present invention obvious. Accordingly, Applications respectfully request withdrawal of the rejection.

Terman and Ruoslahti

The Examiner rejected claims 1 and 3-4 under 35 U.S.C. § 103(a) over Terman (U.S. Pat. No. 6,340,461) in view of Rouslahti (U.S. Pat. No. 6,180,084). The Examiner alleged that the fusion antigen disclosed by Terman combined with the NGR peptide motif of Ruoslahti renders the presently claimed invention obvious. Applicants resepectfully traverse this rejection as it may apply to the amended claims.

The fusion complex of Terman is fundamentally intended to increase the T-cell immune response against the immunotherapeutic antigen to treat cancer and diseases, *not* to trigger a complement-mediated hyperacute immune reaction. *See* col. 3, l. 61 to col. 4, l. This complex comprises superantigens and immunotherapeutic antigens. Superantigens are those proteins that have "the ability to stimulate proliferation [of] a large set of CD4+ T cells by binding to certain Vβ segments of T cell receptors." Col. 5, ll. 27-31. Immunotherapeutic antigens are defined in col. 7, ll. 19-41 as "[antigens that] bind to the T cell receptors of a lymphocyte population." Thus, the complex of Terman is directed to increasing the antigen-specific T cell response, *not* complement-mediated immune response of the present invention. Thus, the claimed invention utilizes a very different pathway than that of the cited references.

Terman discloses the use of gal(alpha1-3)gal determinants in conjunction with "superantigens . . . to further promote T cell activation" Col. 50, ll. 15-16. This complex may be conjugated to an antibody as described in the protocol beginning in col. 52, l. 17. There is

no disclosure of the claimed composition comprising a carrier portion, a complement-triggering portion and a targeting portion. Indeed, Terman teaches the use of an antibody with the fusion molecule, which has been found to be detrimental in the present invention. This further illustrates the difference in the pathways used by Terman and the present invention.

Ruoslahti does not remedy this deficiency, Although Ruoslahti teaches the NGR peptide, the reference does not teach using complement-mediated immune responses to kill tumor cells. Adding the NGR peptide to the immunotherapy-superantigen complex of Terman would still activate the T cell-mediated immune response. Thus, the combined references do not teach each and every element of the claims.

Further, there would be no expectation of success in achieving the present invention if the teachings of the two references were combined as neither reference teaches the triggering of complement-mediated immune reactions.

While Terman mentions the hyperacute rejection process associated with xenograft rejection (*see* col. 51, ll. 39-55), the reference also teaches the use of an antibody in conjunction with the carbohydrate-superantigen complex, which destroys the complement reaction, as disclosed the present application. The present application, however, specifically discourages the use of an antibody because a complement response was not observed. The pending claims also recite that the targeting portion is not an antibody or antibody fragment. Therefore, a person of skill in the art would not have the motivation to combine the cited references to form the present invention as they are directed to eliciting T cell responses, not complement-mediated responses.

Because the cited references in combination do not teach each and every element of the claimed invention, nor would one of skill in the art have any motivation or expectation of success for such a combination to arrive at the present invention, they cannot render the claimed invention obvious. Accordingly, Applicants respectfully request withdrawal of the rejection.

Terman, Ruoslahti and Corti

The Examiner rejects claim 2 under 35 U.S.C. § 103(a) over Terman, Ruoslahti and Corti. Specifically, the Examiner alleges that Corti provides for the addition of human serum albumin to the composition of Terman as modified by Ruoslahti to arrive at the invention of claim 2. Applicants respectfully traverse this rejection.

The deficiencies of the combination of Terman and Ruoslahti have been discussed *supra*. Essentially, the composition would elicit T cell mediated responses, whereas the present invention is directed to compositions eliciting complement-mediated responses. As discussed *supra*, Corti also teaches compositions that trigger a TNF-mediated response, which is distinctly different from the complement-mediated response. Thus, not only does the combination of cited references not teach each and every element of the claims, a person of skill in the art would have no motivation to combine the reference because Corti teaches activation of a pathway that is distinct from those of Terman and Ruoslahti. Therefore, this combination cannot render the claimed invention obvious. Accordingly, Applicants respectfully request withdrawal of the rejection.

Terman, Ruoslahti and Patierno

The Examiner rejects claims 10-17 under 35 U.S.C. § 103(a) over Terman, Ruoslahti and Patierno. The Examiner alleges that the composition of the combination of Terman and Ruoslahti packaged in the kit of Patierno rendered these claims obvious. Applicants respectfully traverse this rejection.

The deficiencies of the combination of Terman and Ruoslahti have already been discussed. Essentially, the composition would elicit T cell mediated responses, whereas the present invention is directed to compositions eliciting complement-mediated responses. As discussed *supra*, Patierno merely discloses kits and does not teach compositions that trigger a complement mediated immune response. Thus, not only does the combination of cited references not teach each and every element of the claims, a person of skill in the art would

have no motivation or expectation of success for such a combination to arrive at the present invention. Therefore, this combination cannot render the claimed invention obvious. Accordingly, Applicants respectfully request withdrawal of the rejection.

Terman, Ruoslahti ,Patierno and Corti

The Examiner rejects claim 18 under 35 U.S.C. § 103(a) over Terman, Ruoslahti, Patierno and Corti. The Examiner alleges that the composition of the combination of Terman and Ruoslahti with the human serum albumin of Corti packaged in the kit of Patierno rendered this claim obvious. Applicants respectfully traverse this rejection.

The deficiencies of the combination of Terman and Ruoslahti have already been discussed. Essentially, the composition would elicit T cell mediated responses, whereas the present invention is directed to compositions eliciting complement-mediated responses. Likewise, Corti teaches compositions that trigger a TNF-mediated response distinctly different from the complement-mediated respons, and Patierno merely discloses kits. None of the cited references teaches compositions that trigger complement-mediated immune responses, only other immune responses. Thus, not only does the combination of cited references not teach each and every element of the claims, a person of skill in the art would have no motivation or expectation of success for such a combination to arrive at the present invention. Therefore, this combination cannot render the claimed invention obvious. Accordingly, Applicants respectfully request withdrawal of the rejection.

Conclusion

Applicant believes that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

Date Feb 26, 2007

By _____

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